PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 11 January 2000 (11.01.00)	
International application No. PCT/GB99/01379	**Applicant's or agent's file reference** GS/P50062WO
International filing date (day/month/year) 18 May 1999 (18.05.99)	**Priority date** (day/month/year) 18 May 1998 (18.05.98)
Applicant FREEMAN, Neville, John et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   10 December 1999 (10.12.99)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia RANAIVOJAONA Telephone No.: (41-22) 338.83.38

E.1

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
GS/P50062WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 99/ 01379	18/05/1999	18/05/1998
Applicant		
FARFIELD SENSORS LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1a

[ ] as suggested by the applicant.

[X] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[ ] None of the figures.

International application No.
PCT/GB 99/01379

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Line 4: replace "Refering to Figure 1a," with "In one embodiment"
Line 12: add "In another embodiment, the apertures take the form of through-holes." after "8."

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/01379

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N27/403

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 585 933 A (MATSUSHITA ELECTRIC INDUSTRIAL) 9 March 1994 (1994-03-09) column 8, line 53 - column 9, line 40 figures 1-3 ---	1-4,6, 16,20, 26,27
X	WO 93 22678 A (MASSACHUSETTS INSTITUTE OF TECHNOLOGY) 11 November 1993 (1993-11-11) page 3, line 21 - page 4, line 25 page 7, line 20 - page 13, line 8 page 24, line 5 - page 31, line 11 page 32, line 17 - page 34, line 8 figures 1-6H,18,19 --- -/--	1-4,6,7, 10,14, 16,18, 19,23, 25-27

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 September 1999	15/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Johnson, K

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	DE 297 17 809 U (KURT-SCHWABE-INSTITUT FÜR MESS- UND SENSORTECHNIK) 5 March 1998 (1998-03-05) the whole document ---	1-4,6, 10, 15-17, 26-28
X	EP 0 102 042 A (TOKYO SHIBAURA ELECTRIC) 7 March 1984 (1984-03-07) page 5, line 1 - page 10, line 18 figures 1-2C ---	1-3,5,7, 9,14-16, 20,26,27
X	HINKERS H ET AL: "Amperometric microelectrode array in containment technology" SENSORS AND ACTUATORS B, vol. B27, no. 1-3, pt II, 1 June 1995 (1995-06-01), pages 398-400, XP000516355 ISSN 0925-4005	1,2,4,6, 8,10,14, 21,23, 26,27
A	page 399, left-hand column, paragraph 2 - right-hand column, line 4, paragraph 3; figure 1 ---	5,15
X	US 4 666 574 A (ODA Y ET AL) 19 May 1987 (1987-05-19) column 2, line 43 - column 7, line 42 figures 1,2 ---	1,2,4,6, 11-13, 21,22,25
A	DE 196 45 653 A (HOSSE H) 7 May 1998 (1998-05-07) abstract; figure 1 ---	1,24
P,X	US 5 824 494 A (FELDBERG S) 20 October 1998 (1998-10-20) column 10, line 33 - line 64; figure 8 -----	1-5,9,26

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 99/01379

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
EP 0585933	A	09-03-1994	JP	6296595	A	25-10-1994
			JP	6078889	A	22-03-1994
			US	5810725	A	22-09-1998
WO 9322678	A	11-11-1993	US	5846708	A	08-12-1998
			EP	0638173	A	15-02-1995
			JP	7508831	T	28-09-1995
			US	5653939	A	05-08-1997
DE 29717809	U	05-03-1998	NONE			
EP 0102042	A	07-03-1984	JP	1606855	C	13-06-1991
			JP	2033981	B	31-07-1990
			JP	59038647	A	02-03-1984
			DE	3376762	A	30-06-1988
			US	4533457	A	06-08-1985
			US	4647362	A	03-03-1987
US 4666574	A	19-05-1987	JP	1051550	B	06-11-1989
			JP	1581594	C	11-10-1990
			JP	57023076	A	06-02-1982
			JP	1322047	C	11-06-1986
			JP	56075583	A	22-06-1981
			JP	59040231	B	28-09-1984
			AU	535261	B	08-03-1984
			AU	6412180	A	04-06-1981
			BR	8007712	A	09-06-1981
			CA	1184883	A	02-04-1985
			CA	1280716	A	26-02-1991
			DE	3044767	A	24-09-1981
			EP	0029751	A	03-06-1981
			GB	2064586	A,B	17-06-1981
			IN	153140	A	02-06-1984
			IT	1141093	B	01-10-1986
			US	4909912	A	20-03-1990
			US	4661218	A	28-04-1987
			SU	1593575	A	15-09-1990
DE 19645653	A	07-05-1998	WO	9819769	A	14-05-1998
US 5824494	A	20-10-1998	NONE			

PATENT COOPERATION TREATY

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RECD 01 SEP 2000
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Ab

Applicant's or agent's file reference GS/AMW/P500602WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/01379	International filing date *(day/month/year)* 18/05/1999	Priority date *(day/month/year)* 18/05/1998
International Patent Classification (IPC) or national classification and IPC G01N27/403		
Applicant FARFIELD SENSORS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 10/12/1999	Date of completion of this report 29.08.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Johnson, K Telephone No. +49 89 2399 2240

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01379

I. Basis of th r port

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-11 as originally filed

Claims, No.:

1-28 as originally filed

Drawings, sheets:

1/5-5/5 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	24
	No:	Claims	1-23,25-28
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-28
Industrial applicability (IA)	Yes:	Claims	1-28
	No:	Claims	

2. Citations and explanations

   see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

   and / or

2. Non-written disclosures (Rule 70.9)

   see separat sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Section IV. Lack of unity of invention

1. The application does not satisfy the requirements of **Rule 13.1 PCT** with regard to unity of invention for the following reasons:

1.1 The common concept linking claims 24-28 together is the microelectrode system defined in claim 1 and dependent claims. However, as demonstrated in section V of this report, the subject matter of claim 1 is not novel. Moreover claim 24 is directed to the use of a microelectrode system for the deionisation of a material; claim 25 to the use of such a system for preparative electrochemistry; and claims 26-28 relate to electroanalysis, in particular as sensors in chromatographic or separation systems. So claims 24, 25 and 26-28 solve different technical problems, and are not linked by any other special technical feature.

1.2 Therefore the technical relationship required by **Rule 13.1 PCT** for unity of invention does not exist between claims 24, 25 and 26-28.

Section V. Reasoned statement under Rule 66.2(a)(ii)

1. The following documents (**D1-D7**), cited in the International Search Report, are referred to in this report:

D1 = EP-A-0585933
D2 = WO-A-9322678
D3 = DE-U-29717809
D4 = SENSORS & ACTUATORS B, June 1995, CH, vol. B27, no. 1/3, pt. II, pages 398-400, ISSN 0925-4005;
Hinkers H et al: ' Amperometric microelectrode array in containment technology'
D5 = EP-A-0102042
D6 = US-A-4666574
D7 = DE-A-19645659

2. Document **D1** discloses (cf. D1, column 8, line 53 - column 9, line 40; figures 1-3) a microelectrode system comprising a laminated structure having at least one conducting layer (2) capable of acting as an electrode, at least one dielectric

layer (4), an aperture (5) formed in the laminated structure, and contact means (7,8) for allowing electrical contact with at least one conducting layer. So the subject matter of claim 1 has been anticipated by this prior art, and the claim does not meet the requirements of **Article 33(2) PCT**.

2.1 Since a similar argument can be derived from each of documents **D2** - **D4**, these documents must also be regarded as novelty destroying for claim 1 (cf. D2, page 3, line 21 - page 4, line 25; page 7, line 20 - page 13, line 8; figures 1-6H, D3, whole document; D4, page 399, left-hand column, paragraph 2 - right-hand column, paragraph 3; figure 1).

2.2 Moreover, it follows from the definition of a microelectrode given in document **D3** (cf. D3, page 1, paragraph 2 'Mikroelektroden sind definiert...') that the electrode systems taught in documents **D5** and **D6** also fall within the scope of claim 1, because the thickness of the electrodes in each case lies in the micrometre range (cf. D5, page 5, line 1 - page 10, line 18; figures 1-2C; D6, column 2, line 43 - column 7, line 42; figures 1,2). So the subject matter of claim 1 is not new over these documents either.

3. Nor do the additional features introduced by dependent claims 2-23 appear to provide the basis for new and inventive subject matter. This is because these features have already been employed for the same purposes in the prior art, else can only be regarded as obvious alternatives to the measures adopted there:

3.1 Thus documents **D1-D6** all disclose[1] apertures which form a uniform wall in the laminate structure (cf. claim 2). Document **D2** also teaches the use of non-uniform walls (cf. D2, page 13, lines 1-8; figure 6H). A tubular internal wall is taught in documents **D3** and **D5**. In any case, such a feature is obvious in the light of the square apertures used in documents **D1** and **D2** (cf. claim 3). Plural apertures are disclosed in each of the documents **D1-D4** and **D6** (cf. claim 4).

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[1]where no specific reference is given, please refer to the passages already cited in the corresponding documents.

3.2 The electrode system of document **D5** consists of a laminated structure with a central bore or through hole (20), which is open at both ends. Through holes are also formed in the manufacture of the microelectrode array known from document **D4** (cf. claim 5). Wells as specified in claim 6 are known from documents **D1-D4** and **D6**.

3.3 In document **D2**, probe molecules are attached to the electrodes (cf. D2, page 24, line 5 - page 31, line 11). Also an ion selective layer is applied to the electrode surfaces in document **D5**. So these documents advocate functionalising at least one conductive layer (cf. claim 7).

3.4 Document **D4** teaches the use of a hydrogel as electrolyte, ie. the microelectrode system employs a rubbery material which swells in the presence of a liquid (cf. claims 8, 21). In document **D5**, consecutive conducting layers are separated by dielectric layers (cf. claims 9, 20). A silicon base is used for constructing the laminate structure in documents **D2** and **D4**, whereas **D4** employs polymeric material (cf. claim 10).

3.5 The openings in the electrode mesh (4,5) applied on both sides of the ion exchange membrane (1) in document **D6** give rise to a plurality of pairs of substantially collinear wells having a common well bottom made from ion exchange material. So the features of claims 11-13 are also known from this prior art. A similar conclusion holds for claims 21 and 22, insofar as a potential is applied across a specialised ion exchange layer.

3.6 In documents **D2** and **D5**, a conducting, metallic layer is treated with an organic conducting layer (cf. claim 14). Furthermore, the electrode system of **D5** includes a silver/silver chloride reference electrode. In any case, document **D3** discloses the use of a reference electrode. As the skilled person is well aware, silver/silver chloride represents an obvious choice for implementing such a reference electrode (cf. claim 15). A gold conducting layer is employed in documents **D1-D3** and **D5** (cf. claim 16). In document **D3**, the gold layer is supported on a polymeric substrate (cf. claim 17).

3.7 A microfluidic flow system, including a piezoelectric actuator, is employed in the system known from document **D2** to assist mass flow (cf. D2, page 32, line 17 - page 34, line 8; figures 18, 19). So the subject matter of claims 18 and 19 is just state of the art. Finally the features of claim 23 are known from documents **D2** and **D4**.

3.8 Therefore the adoption of these features, either singly or in combination, would not betoken inventive skill.

4. Independent claim 24 is directed to the use of a microelectrode system for the deionisation of a material. Document **D7** discloses an electrode system for water softening, ie the deionisation of water (cf. D7, abstract, figure 1). An obvious way of constructing the apparatus shown in figure 1 of this document would be to employ the technology taught in document **D5**. In this way the skilled person would arrive at subject matter falling within the ambit of claim 24. Therefore claim 24 does not meet the requirements of **Article 33(3) PCT** with regard to inventive step.

5. Document **D2** teaches the use of the microelectrode array for preparing the probe species at each test site. Similarly the system known from document **D6** is intended for the production of alkali metal hydroxides. Therefore the subject matter of claim 25, directed to the use of a microelectrode system for preparative electrochemistry, is not novel. Also, the microelectrode system advocated in document **D3** is especially intended for electroanalytical purposes, in particular in chromatography and voltammetry. So document **D3** takes away the novelty of claims 26-28.

Section VI. Certain documents

Certain published documents (**Rule 70.10 PCT**)

1. The American patent document listed below:

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim) (day/month/year)*
US-A-5824494	20.10.1998	26.04.1995	01.05.1994

discloses all the features of claims 1-5, 9 and 26 (cf. column 10, line 33 - column 64, figure 8). However, the document was published after the relevant date for assessing novelty and inventive step (cf. **Rule 64.1 PCT**)

Section VII. Certain defects in the International Application

The following defects in the form or contents of the international application have been noted:

1. Contrary to the requirements of **Rule 5.1(a)(ii) PCT**, the relevant background art disclosed in the documents **D1-D7** has not been mentioned in the description, nor have these documents been identified therein.

2. Independent claims 1, 24-26 have not been drafted in the two part form recommended in **Rule 6.3(b) PCT**, although this would have been appropriate in the light of the prior art discussed above.

3. The features of the claims have not been have not been identified by reference signs placed in parentheses, as recommended in **Rule 6.2(b) PCT**.

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G01N 27/403

A1

(11) International Publication Number: WO 99/60392

(43) International Publication Date: 25 November 1999 (25.11.99)

(21) International Application Number: PCT/GB99/01379

(22) International Filing Date: 18 May 1999 (18.05.99)

(30) Priority Data:
9810568.7 18 May 1998 (18.05.98) GB

(71) Applicant (*for all designated States except US*): FARFIELD SENSORS LIMITED [GB/GB]; Commonwealth House, Room 4009, 4th floor, Chicago Avenue, Manchester Airport, Manchester M90 3DQ (GB).

(72) Inventors; and
(75) Inventors/Applicants (*for US only*): FREEMAN, Neville, John [GB/GB]; 7 Croft Close, Utkinton, Tarporley CW6 0XA (GB). MOUNT, Andrew [GB/GB]; 18 Cambee End, Libberton, Edinburgh EH16 6GJ (GB).

(74) Agents: STUTTARD, Garry, Philip et al.; Urquhart-Dykes & Lord, Tower House, Merrion Way, Leeds LS2 8PA (GB).

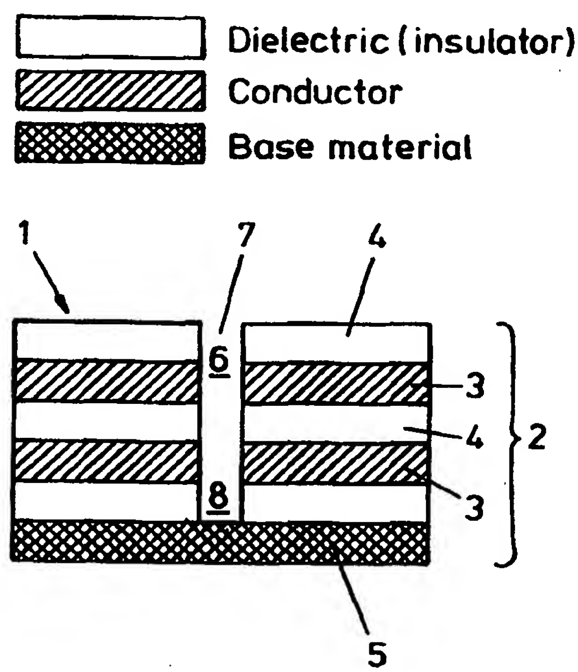
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: MICROELECTRODE SYSTEM

(57) Abstract

A microelectrode system suitable for use in preparative and analytical chemistry having a laminated structure with one or more apertures. In one embodiment a microelectrode system (1) comprises alternating layers of conductor (3) and dielectric (or insulator) (4). The laminated structure (2) comprises two conductor layers (3) and two dielectric layers (4) formed on a base (5) of silicon or a polymeric material. The conducting layers (3) form electrodes in the microelectrodes system (1). The laminated structure has formed within it an aperture in the form of a well (6) being open at one end (7) and closed at the opposite end (8). In another embodiment, the apertures take the form of through holes.



Microelectrode system

The present invention relates to an electrode system, and particularly to a microelectrode system suitable for use in preparative and analytical chemistry.

Microelectrode systems are used extensively in research and are so named because their dimensions are on the micrometre scale. Such microelectrode systems provide very high field gradients and diffusion characteristics due to their small size. In addition, these types of microelectrode systems have found some limited commercial utility in biomedical applications and are typically used in, for example, blood gas analysis.

Reliable operation of microelectrode systems for preparative electrochemistry and electroanalytical techniques depends critically upon their geometry and the reproducibility of their manufacture. The performance of such a system generally improves as the dimensions of the system are reduced which is why microelectrode and even nanometre scale microelectrode systems are often desirable.

A disadvantage of known microelectrode systems of this type is that the reproducibility and reliability of the fabrication process and the geometries which may be adopted become more limited as the scale is reduced.

The present invention seeks to provide an improved microelectrode system which is more straightforwardly and reproducibly manufactured irrespective of dimensionality.

Thus viewed from one aspect the present invention provides a microelectrode system comprising a laminated structure having at least one conducting layer capable of acting as an electrode, at least one dielectric layer, an aperture formed in the laminated structure, and contact means for allowing electrical contact with at least one conducting layer.

As the dimensions of the microelectrode system of the invention are extremely small, the fields generated within the laminated structure are exceptional and enable highly efficient measurement and/or modification of materials entering into or passing through the system. The laminated structure is simple to manufacture to extremely high tolerances. In addition, the structure has extremely low dead volume thereby considerably simplifying physical sampling regimes.

The aperture may be in the form of a hole which extends through the laminated structure and is open at both ends. Alternatively, the aperture may be in the form of a well having an open end and an opposite end being closed to form a well bottom. In both embodiments, the internal wall of the hole or well formed in the microelectrode system may be uniform (*eg* substantially tubular) or non-uniform to provide non-uniform fields if desired. Materials may be passed into or through the laminated structure (via the aperture) where *inter alia* synthesis, analysis or sequencing as desired takes place.

The microelectrode system of the invention may comprise a plurality of apertures (*eg* holes or wells) formed within the laminated structure and spaced apart from one another. Each hole or well may be individually addressable, in which case each hole or well may have a different function. Alternatively, groups of holes or wells (or the totality of the holes or wells) in a structure may be addressed in parallel thereby enabling amplification of signals and parallel material processing. This latter system may be suitable for larger scale synthetic applications.

In one embodiment, the microelectrode system comprises at least one pair of substantially collinear wells having a common closed end. Particularly preferably, the microelectrode system comprises a plurality of such pairs.

At least one conducting layer of the microelectrode system of the invention acts as an electrode on the internal wall of the hole or well. The or each electrode may be treated

to provide appropriate functionality (*eg* pH measurement or surface treatment for electro-catalysis) by known chemical and/or electrochemical and/or physical modification techniques.

The laminated structure may comprise a plurality of conducting and a plurality of dielectric layers. Preferably consecutive conducting layers are separated by dielectric layers. Particularly preferably, a dielectric layer is uppermost in the laminated structure. In one embodiment, the laminated structure preferably comprises three conducting layers. Electrical fields are generated between the layers forming the laminated structure and within the aperture to provide the desired conditions.

Typically, the electrodes are formed from a noble metal, preferably gold. Gold may be sputtered onto a polymer which is capable of acting both as the mechanical support and as the dielectric layer. Any form of polymer or other dielectric material which is capable of acting as a support may be used such as for example polyethylenetetraphthalate (PET). Other specialised materials such as ion exchange polymers (*eg* cation doped polystyrene sulphonate) may be used for specialised applications.

Advantageously, the or each dielectric layer is made from a rubbery material. A suitable material is a polymer which swells when molecules of (for example) water enter the solid state matrix. During use of the microelectrode system, the rubbery dielectric layers separating pairs of conducting layers swell thereby changing the inter-electrode distance. Thus, the interspaced electrodes may be interrogated to determine the degree of swelling of the dielectric layers as a function of the measured resistance.

In more complex systems, material may be grown between the or each conducting layer and the or each rubbery dielectric layer, and the stress placed on the material as a consequence of the swelling of the or each dielectric layer may be measured.

A reagent loaded or functionalised dielectric layer may be used to provide additional functionality by providing ions or other materials to ensure the reproducible behaviour of subsequent systems within the structure. Ions may be conveniently provided by ion exchange resin materials. Other matrices could be employed to provide co-factors for biosensors, etc.

A specialised dielectric layer may also be used. The specialised layer may be in the form of an ion exchange resin, gel or solid electrolyte. In such a system, mass transport from one lateral region of the structure to another may be effected by *inter alia* osmosis, electro-osmosis, electrophoresis, electrochromatography or ion migration. Reverse flow and counter current techniques may be employed to effect changes in process flows including *inter alia* deionisation.

The laminated structure may be built on silicon. This has the advantage of being optically flat. Alternatively, the laminated structure may be built on a polymeric material (*eg* a polymeric material comprising one or more polymers).

The layers forming the laminated structure may be laid down using any one of a number of known techniques including casting, spinning, sputtering or vapour deposition methods. The aperture may be mechanically or chemically introduced into the laminated structure. Advantageously, a micron gauge wire made of (for example) silver may be introduced into the laminated structure which wire may be etched out once the laminar structure has been completed. Alternatively, lithographic techniques or physical techniques such as laser oblation and neutron annihilation may be used. It is possible to produce highly uniform electrode layers with precise separations using such techniques allowing highly reproducible functional structures to be achieved.

The microelectrode system of the invention has many applications. For example, it may be used in the deionisation

of a solution positioned on one side of a membrane forming the closed end of a well. In such a case, ions may be pumped through the microelectrode system as a consequence of a potential difference applied to electrodes on either side of the common well bottom. In such a case, the well bottom may be conveniently formed from an ion exchange material. The microelectrode may also be used in preparative electrochemistry, electroanalysis and chromatography or other separation techniques. It may also be used as a sensor.

Where the aperture is in the form of a through hole, the microelectrode system according to the present invention may be used in preparative electrochemistry. In such a case, the reactants on one side of the electrode structure are passed through the hole using (for example) a pressure gradient. As they pass through the holes, the reactants are modified by the applied electric field within each hole, either producing the product directly or generating intermediates which undergo further reaction to form the desired product.

If, for example, the microelectrode system was required to have biological functionality for use in an enzyme or antibody system, the electrodes may be formed from metal treated with an organic conducting layer to prevent the activity of the biological agent from being destroyed.

A silver conducting layer may be used which itself may be chloridised to form a silver/silver chloride reference electrode if desired.

The dimensions of the layers and hole or well forming the microelectrode system may be tailored as desired. The precise dimensions of the microelectrode system depend upon the materials used and the techniques employed to form the microelectrode system.

The diameter of the hole or well is typically in the range 0.5 to 500 microns, preferably 1 to 200 microns, particularly preferably 2 to 10 microns, especially preferably about 5 microns.

The thickness of the or each dielectric layer may be in the range 0.5 to 10000 microns, preferably 0.5 to 1000 microns, particularly preferably 1 to 1000 microns, especially preferably 1 to 60 microns, more especially preferably 1 to 10 microns. Where the dielectric is uppermost or intermediate in the laminated structure, the thickness is typically about 5 microns. Where the dielectric is on the base of the laminated structure, the thickness is typically about 55 microns.

The thickness of the or each conducting layer may be in the range 0.5 to 500 microns, preferably 1 to 100 microns, particularly preferably 1 to 10 microns, especially preferably about 3 microns.

At a location remote from the hole or well is provided a means to enable electrical contact with the or each of the conducting layers. One such means of providing electrical contact would be to slice back the outer edges of the dielectric layers thereby exposing the extreme ends of each of the conducting layers. These exposed ends allow electrical contact to be made.

When a microelectrode system according to the present invention is used in a mass transport system, the potential difference created causes diffusion of desired chemical species to the hole or well. In some cases (for whatever reason) this process is slow and the mass transport may be aided through use of *inter alia* a piezo-electric vibrator or an ultrasonic probe. Mass transport may be additionally controlled (where required) by conventional macroscopic means used in electrochemistry. These techniques include membrane and diffusion, wall jet/wall pipe techniques, rotation, vibration, etc. In the case of a microelectrode system having a through hole, the mass flow may additionally be controlled using differential pressure techniques.

The microelectrode system according to the invention may be in the form a substantially one-dimensional array (*eg* a tape) or a multi-dimensional array (*eg* a sheet or more complex

matrix) to enable repeated measurements with single use systems.

Preferably, the microelectrode system of the invention further comprises a microheater structure incorporated into the system to control local conditions. Preferably, the microheater is in the form of a resistive element laid down using known semi-conductor techniques. The resistive element may provide localised heating.

The invention will now be further described by way of example only with reference to the accompanying drawings in which:

Figure 1a is a schematic representation of an microelectrode system according to the invention incorporating a well;

Figure 1b is a schematic representation of an microelectrode system according to the invention incorporating a through hole;

Figure 2a is a schematic representation of an microelectrode system according to the invention having three electrodes and incorporating a well;

Figure 2b is a schematic representation of an microelectrode system according to the invention having three electrodes and incorporating a through hole;

Figure 3 is a schematic three-dimensional representation of an microelectrode system according to the present invention incorporating two electrodes and a through hole;

Figure 4a is a schematic representation of an microelectrode system according to the invention incorporating two electrodes, a reagent-loaded or functionalised dielectric and a well;

Figure 4b is a schematic representation of an microelectrode system according to the invention incorporating two electrodes, a reagent loaded or functionalised dielectric, and a through hole;

Figures 5a (side elevation) and 5b (plan) are schematic representations of an microelectrode system according to the invention incorporating a specialised or functionalised layer structure;

Figure 6 is a schematic representation of a microelectrode system according to the invention forming a membrane transport system;

Figure 7 is a schematic representation of a microelectrode system according to the invention forming an impedance imaging system; and

Figures 8a and 8b illustrate preferred embodiments of microelectrodes of the invention.

Referring to Figure 1a, a microelectrode system 1 comprises alternating layers of conductor 3 and dielectric (or insulator) 4. The laminated structure 2 comprises two conductor layers 3 and two dielectric layers 4 formed on a base 5 of silicon or a polymeric material. The conducting layers 3 form electrodes in the microelectrode system 1. The laminated structure has formed within it an aperture in the form of a well 6 being open at one end 7 and closed at the opposite end 8.

The microelectrode system 10 shown in Figure 1b has formed within the laminated structure 2 a through hole 11 and comprises three dielectric layers 4 and two conducting layers 3.

Figures 2a and 2b illustrate microelectrode systems 20 and 30 respectively which are similar to the microelectrode systems 1, 10 with similar reference numerals retained to avoid confusion. Each of the microelectrode systems 20, 30 comprises three conducting (electrode) layers 3 and three dielectric layers 4. Hole 11 (Figure 2b) or well 7 (Figure 2a) define an internal wall formed from alternating layers of insulating and conducting material. This produces a circular micro-band microelectrode system in the form of a uniform tube. This can be seen more clearly with reference to Figure 3 which is a

three-dimensional representation of the microelectrode system 10 of Figure 1b.

Materials passing into the structure may be pre-treated. A system suitable for pretreatment of material is shown in Figures 4a and 4b (where parts equivalent to those in Figures 1a and 1b have been given equivalent reference numerals). The microelectrode systems 50, 60 contain two electrode layers 3, two dielectric layers 4 and a reagent loaded or functionalised dielectric layer 5. The reagent loaded or functionalised dielectric layer 5 is able to provide additional functionality by providing ions or other materials to ensure the reproducible behaviour of subsequent systems within the structure. Ions could be provided by ion exchange resin materials. Other matrices could be employed to provide co-factors for biosensors, etc. The layer 5 could act as a buffer if, for example, there was some kind of ion exchange taking place where a remote reservoir was replenishing the ions exchanged within the medium in contact with the membrane.

Referring now to Figure 5a and 5b, a microelectrode system according to the invention is designated generally by the reference numeral 70 with parts equivalent to those shown in Figure 1b given equivalent reference numerals. The microelectrode system 70 comprises a specialised layer 13 between two electrode layers 3. The system further comprises means 14 to produce physical or chemical gradients or potentials to the specialised layer 13. The specialised layer 13 may be in the form of an ion exchange resin, gel or solid electrolyte. In such a system 70 mass transport from one lateral region of the structure to another may be effected by, for example, osmosis, electro-osmosis, electrophoresis, electrochromatography, ion migration, etc. Reverse flow and counter current techniques may be employed to effect changes in process flows including *inter alia* deionisation.

In Figure 6, a microelectrode system 80 suitable for use in deionisation of a solution is designated generally by the

reference numeral 80. The microelectrode system 80 comprises a plurality of wells 82. Each of the wells 82 is split into pairs by the presence of a continuous layer 84 which serves as a common well bottom for each pair. The well bottom is formed from an ion exchange material. Electrodes on either side of the well-bottom generate a potential gradient which forces ions to move across the membrane. This system may be used to deionise water.

Figure 7 illustrates a microelectrode system suitable for impedance imaging (*eg* mammography). It comprises alternating conducting 3 and dielectric layers 4 with a gold overplating 71 which is contactable with the skin for example. It is not important in this embodiment for the overplating material to contact in the centre of the hole. The overplating adopts a shape according to local variations in the environment. Provided the plating extends beyond the hole or well to the upper surface thereby allowing electrical contact to be made with an external surface, the shape and size is not critical. The overplating may be applied by standard electroplating methods (electrochemical methods).

Figures 8a and 8b illustrate embodiments of the invention of the hole-type and well-type respectively. Dielectric layers are made from poly(ethylenetetraphthalate) and conducting layers from gold. The detailed construction of each embodiment is given in the following tables (typical ranges are given for illustrative purposes only):

1) Hole Structure (Figure 8a)

Dimensions (in microns):

Description	Letter	Dimension	Typical Range
Aperture	A	5	0.5 - 500

Description	Letter	Dimension	Typical Range
First dielectric layer	B	5	1 - 1000
First conducting layer	C	3	0.5 - 500
Second dielectric layer	D	5	0.5 - 1000
Second conducting layer	E	3	0.5 - 500
Third dielectric layer	F	5	1 - 1000

2) Well structure (Figure 8b)

Dimensions (in microns):

Description	Letter	Dimension	Typical Range
Aperture	A	5	0.5 - 500
First Dielectric layer	B	5	1 - 1000
First conducting layer	C	3	0.5 - 500
Second dielectric layer	D	5	0.5 - 1000
Second conducting layer	E	3	0.5 - 500
Third dielectric layer	F	55	1 - 10000

CLAIMS:

1. A microelectrode system comprising a laminated structure having at least one conducting layer capable of acting as an electrode, at least one dielectric layer, an aperture formed in the laminated structure, and contact means for allowing electrical contact with at least one conducting layer.

2. A microelectrode system as claimed in claim 1 wherein said aperture defines a uniform or non-uniform internal wall in the laminate structure.

3. A microelectrode system as claimed in claim 1 or 2 wherein said aperture defines a substantially tubular internal wall in the laminate structure.

4. A microelectrode system as claimed in any preceding claim comprising a plurality of apertures.

5. A microelectrode system as claimed in any preceding claim wherein said aperture is a through hole which extends through the laminated structure and is open at both ends.

6. A microelectrode system as claimed in any of claims 1 to 4 wherein the aperture is in the form of a well having an open end and an opposite end being closed to form a well bottom.

7. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer is functionalised.

8. A microelectrode system as claimed in any preceding claim wherein at least one dielectric layer is made from a

rubbery material having a solid state matrix capable of swelling in the presence of a liquid or gas.

9. A microelectrode system as claimed in any preceding claim wherein consecutive conducting layers are separated by dielectric layers.

10. A microelectrode system as claimed in any preceding claim wherein the laminate structure is constructed on a base comprising silicon or a polymeric material.

11. A microelectrode system as claimed in any preceding claim comprising at least one pair of substantially collinear wells having a common well bottom.

12. A microelectrode system as claimed in claim 11 comprising a plurality of pairs of substantially collinear wells having a common well bottom.

13. A microelectrode system as claimed in claim 11 or 12 wherein said well bottom is formed from an ion exchange material.

14. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer is metallic and treated with an organic conducting layer.

15. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer is a silver/silver chloride reference electrode.

16. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer consists essentially of gold.

17. A microelectrode system as claimed in claim 16, wherein at least one dielectric layer is polymeric and acts as a support for the gold conducting layer.

18. A microelectrode system as claimed in any preceding claim comprising means for assisting mass transport.

19. A microelectrode system as claimed in claim 18 wherein said means for assisting mass transport is a piezoelectric vibrator or ultrasonic probe.

20. A microelectrode system as claimed in any preceding claim comprising alternating conducting and dielectric layers.

21. A microelectrode system as claimed in any preceding claim wherein at least one dielectric layer comprises a specialised layer in the form of an ion exchange resin, gel or solid electrolyte.

22. A microelectrode system as claimed in claim 21 wherein the specialised layer is provided with means to apply physical or chemical gradients or potentials thereto.

23. A microelectrode system as claimed in any preceding claim wherein at least one dielectric layer comprises a reagent loaded or functionalised layer.

24. Use of a microelectrode system as claimed in any preceding claim for deionisation of a material.

25. Use of a microelectrode system as claimed in any of claims 1 to 23 for use in preparative electrochemistry.

26. Use of a microelectrode system as claimed in any of claims 1 to 23 for use in electroanalysis.

27. Use of a microelectrode system as claimed in any of claims 1 to 23 for use as a sensor.

28. Use of a microelectrode system as claimed in any of claims 1 to 23 for use in chromatography or separation techniques.

INTERNATIONAL SEARCH REPORT

International Application No
PC./GB 99/01379

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N27/403

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 585 933 A (MATSUSHITA ELECTRIC INDUSTRIAL) 9 March 1994 (1994-03-09) column 8, line 53 - column 9, line 40 figures 1-3	1-4,6,16,20,26,27
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 September 1999	15/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Johnson, K

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International Application No
PC./GB 99/01379

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

International Application No
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09/700649.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 November 1999 (25.11.1999)

PCT

(10) International Publication Number
WO 99/60392 A1

(51) International Patent Classification[6]: G01N 27/403

(21) International Application Number: PCT/GB99/01379

(22) International Filing Date: 18 May 1999 (18.05.1999)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9810568.7 18 May 1998 (18.05.1998) GB

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(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.

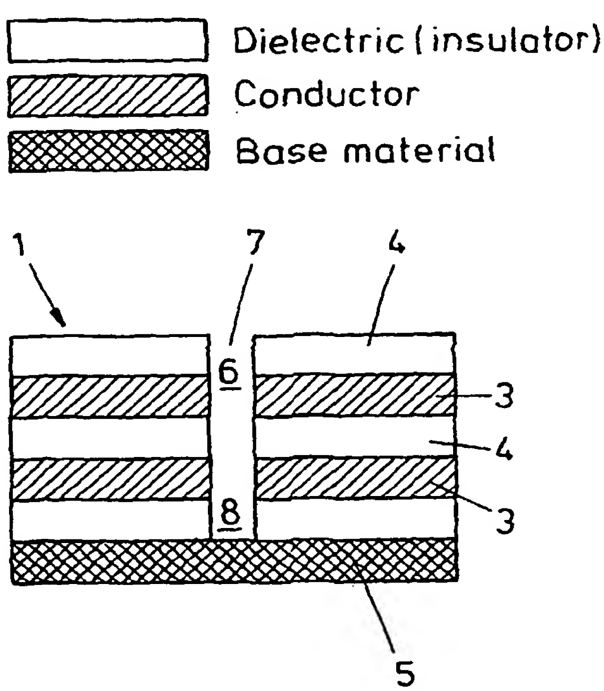
(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

(48) Date of publication of this corrected version:
5 April 2001

[Continued on next page]

(54) Title: MICROELECTRODE SYSTEM



(57) Abstract: A microelectrode system suitable for use in preparative and analytical chemistry having a laminated structure with one or more apertures. In one embodiment a microelectrode system (1) comprises alternating layers of conductor (3) and dielectric (or insulator) (4). The laminated structure (2) comprises two conductor layers (3) and two dielectric layers (4) formed on a base (5) of silicon or a polymeric material. The conducting layers (3) form electrodes in the microelectrodes system (1). The laminated structure has formed within it an aperture in the form of a well (6) being open at one end (7) and closed at the opposite end (8). In another embodiment, the apertures take the form of through holes.

WO 99/60392 A1

(15) Information about Correction:
see PCT Gazette No. 14/2001 of 5 April 2001, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Microelectrode system

The present invention relates to an electrode system, and particularly to a microelectrode system suitable for use in preparative and analytical chemistry.

Microelectrode systems are used extensively in research and are so named because their dimensions are on the micrometre scale. Such microelectrode systems provide very high field gradients and diffusion characteristics due to their small size. In addition, these types of microelectrode systems have found some limited commercial utility in biomedical applications and are typically used in, for example, blood gas analysis.

Reliable operation of microelectrode systems for preparative electrochemistry and electroanalytical techniques depends critically upon their geometry and the reproducibility of their manufacture. The performance of such a system generally improves as the dimensions of the system are reduced which is why microelectrode and even nanometre scale microelectrode systems are often desirable.

A disadvantage of known microelectrode systems of this type is that the reproducibility and reliability of the fabrication process and the geometries which may be adopted become more limited as the scale is reduced.

The present invention seeks to provide an improved microelectrode system which is more straightforwardly and reproducibly manufactured irrespective of dimensionality.

Thus viewed from one aspect the present invention provides a microelectrode system comprising a laminated structure having at least one conducting layer capable of acting as an electrode, at least one dielectric layer, an aperture formed in the laminated structure, and contact means for allowing electrical contact with at least one conducting layer.

As the dimensions of the microelectrode system of the invention are extremely small, the fields generated within the laminated structure are exceptional and enable highly efficient measurement and/or modification of materials entering into or passing through the system. The laminated structure is simple to manufacture to extremely high tolerances. In addition, the structure has extremely low dead volume thereby considerably simplifying physical sampling regimes.

The aperture may be in the form of a hole which extends through the laminated structure and is open at both ends. Alternatively, the aperture may be in the form of a well having an open end and an opposite end being closed to form a well bottom. In both embodiments, the internal wall of the hole or well formed in the microelectrode system may be uniform (*eg* substantially tubular) or non-uniform to provide non-uniform fields if desired. Materials may be passed into or through the laminated structure (via the aperture) where *inter alia* synthesis, analysis or sequencing as desired takes place.

The microelectrode system of the invention may comprise a plurality of apertures (*eg* holes or wells) formed within the laminated structure and spaced apart from one another. Each hole or well may be individually addressable, in which case each hole or well may have a different function. Alternatively, groups of holes or wells (or the totality of the holes or wells) in a structure may be addressed in parallel thereby enabling amplification of signals and parallel material processing. This latter system may be suitable for larger scale synthetic applications.

In one embodiment, the microelectrode system comprises at least one pair of substantially collinear wells having a common closed end. Particularly preferably, the microelectrode system comprises a plurality of such pairs.

At least one conducting layer of the microelectrode system of the invention acts as an electrode on the internal wall of the hole or well. The or each electrode may be treated

to provide appropriate functionality (*eg* pH measurement or surface treatment for electro-catalysis) by known chemical and/or electrochemical and/or physical modification techniques.

The laminated structure may comprise a plurality of conducting and a plurality of dielectric layers. Preferably consecutive conducting layers are separated by dielectric layers. Particularly preferably, a dielectric layer is uppermost in the laminated structure. In one embodiment, the laminated structure preferably comprises three conducting layers. Electrical fields are generated between the layers forming the laminated structure and within the aperture to provide the desired conditions.

Typically, the electrodes are formed from a noble metal, preferably gold. Gold may be sputtered onto a polymer which is capable of acting both as the mechanical support and as the dielectric layer. Any form of polymer or other dielectric material which is capable of acting as a support may be used such as for example polyethylenetetraphthalate (PET). Other specialised materials such as ion exchange polymers (*eg* cation doped polystyrene sulphonate) may be used for specialised applications.

Advantageously, the or each dielectric layer is made from a rubbery material. A suitable material is a polymer which swells when molecules of (for example) water enter the solid state matrix. During use of the microelectrode system, the rubbery dielectric layers separating pairs of conducting layers swell thereby changing the inter-electrode distance. Thus, the interspaced electrodes may be interrogated to determine the degree of swelling of the dielectric layers as a function of the measured resistance.

In more complex systems, material may be grown between the or each conducting layer and the or each rubbery dielectric layer, and the stress placed on the material as a consequence of the swelling of the or each dielectric layer may be measured.

A reagent loaded or functionalised dielectric layer may be used to provide additional functionality by providing ions or other materials to ensure the reproducible behaviour of subsequent systems within the structure. Ions may be conveniently provided by ion exchange resin materials. Other matrices could be employed to provide co-factors for biosensors, etc.

A specialised dielectric layer may also be used. The specialised layer may be in the form of an ion exchange resin, gel or solid electrolyte. In such a system, mass transport from one lateral region of the structure to another may be effected by *inter alia* osmosis, electro-osmosis, electrophoresis, electrochromatography or ion migration. Reverse flow and counter current techniques may be employed to effect changes in process flows including *inter alia* deionisation.

The laminated structure may be built on silicon. This has the advantage of being optically flat. Alternatively, the laminated structure may be built on a polymeric material (*eg* a polymeric material comprising one or more polymers).

The layers forming the laminated structure may be laid down using any one of a number of known techniques including casting, spinning, sputtering or vapour deposition methods. The aperture may be mechanically or chemically introduced into the laminated structure. Advantageously, a micron gauge wire made of (for example) silver may be introduced into the laminated structure which wire may be etched out once the laminar structure has been completed. Alternatively, lithographic techniques or physical techniques such as laser oblation and neutron annihilation may be used. It is possible to produce highly uniform electrode layers with precise separations using such techniques allowing highly reproducible functional structures to be achieved.

The microelectrode system of the invention has many applications. For example, it may be used in the deionisation

of a solution positioned on one side of a membrane forming the closed end of a well. In such a case, ions may be pumped through the microelectrode system as a consequence of a potential difference applied to electrodes on either side of the common well bottom. In such a case, the well bottom may be conveniently formed from an ion exchange material. The microelectrode may also be used in preparative electrochemistry, electroanalysis and chromatography or other separation techniques. It may also be used as a sensor.

Where the aperture is in the form of a through hole, the microelectrode system according to the present invention may be used in preparative electrochemistry. In such a case, the reactants on one side of the electrode structure are passed through the hole using (for example) a pressure gradient. As they pass through the holes, the reactants are modified by the applied electric field within each hole, either producing the product directly or generating intermediates which undergo further reaction to form the desired product.

If, for example, the microelectrode system was required to have biological functionality for use in an enzyme or antibody system, the electrodes may be formed from metal treated with an organic conducting layer to prevent the activity of the biological agent from being destroyed.

A silver conducting layer may be used which itself may be chloridised to form a silver/silver chloride reference electrode if desired.

The dimensions of the layers and hole or well forming the microelectrode system may be tailored as desired. The precise dimensions of the microelectrode system depend upon the materials used and the techniques employed to form the microelectrode system.

The diameter of the hole or well is typically in the range 0.5 to 500 microns, preferably 1 to 200 microns, particularly preferably 2 to 10 microns, especially preferably about 5 microns.

The thickness of the or each dielectric layer may be in the range 0.5 to 10000 microns, preferably 0.5 to 1000 microns, particularly preferably 1 to 1000 microns, especially preferably 1 to 60 microns, more especially preferably 1 to 10 microns. Where the dielectric is uppermost or intermediate in the laminated structure, the thickness is typically about 5 microns. Where the dielectric is on the base of the laminated structure, the thickness is typically about 55 microns.

The thickness of the or each conducting layer may be in the range 0.5 to 500 microns, preferably 1 to 100 microns, particularly preferably 1 to 10 microns, especially preferably about 3 microns.

At a location remote from the hole or well is provided a means to enable electrical contact with the or each of the conducting layers. One such means of providing electrical contact would be to slice back the outer edges of the dielectric layers thereby exposing the extreme ends of each of the conducting layers. These exposed ends allow electrical contact to be made.

When a microelectrode system according to the present invention is used in a mass transport system, the potential difference created causes diffusion of desired chemical species to the hole or well. In some cases (for whatever reason) this process is slow and the mass transport may be aided through use of *inter alia* a piezo-electric vibrator or an ultrasonic probe. Mass transport may be additionally controlled (where required) by conventional macroscopic means used in electrochemistry. These techniques include membrane and diffusion, wall jet/wall pipe techniques, rotation, vibration, etc. In the case of a microelectrode system having a through hole, the mass flow may additionally be controlled using differential pressure techniques.

The microelectrode system according to the invention may be in the form a substantially one-dimensional array (*eg* a tape) or a multi-dimensional array (*eg* a sheet or more complex

matrix) to enable repeated measurements with single use systems.

Preferably, the microelectrode system of the invention further comprises a microheater structure incorporated into the system to control local conditions. Preferably, the microheater is in the form of a resistive element laid down using known semi-conductor techniques. The resistive element may provide localised heating.

The invention will now be further described by way of example only with reference to the accompanying drawings in which:

Figure 1a is a schematic representation of an microelectrode system according to the invention incorporating a well;

Figure 1b is a schematic representation of an microelectrode system according to the invention incorporating a through hole;

Figure 2a is a schematic representation of an microelectrode system according to the invention having three electrodes and incorporating a well;

Figure 2b is a schematic representation of an microelectrode system according to the invention having three electrodes and incorporating a through hole;

Figure 3 is a schematic three-dimensional representation of an microelectrode system according to the present invention incorporating two electrodes and a through hole;

Figure 4a is a schematic representation of an microelectrode system according to the invention incorporating two electrodes, a reagent-loaded or functionalised dielectric and a well;

Figure 4b is a schematic representation of an microelectrode system according to the invention incorporating two electrodes, a reagent loaded or functionalised dielectric, and a through hole;

Figures 5a (side elevation) and 5b (plan) are schematic representations of an microelectrode system according to the invention incorporating a specialised or functionalised layer structure;

Figure 6 is a schematic representation of a microelectrode system according to the invention forming a membrane transport system;

Figure 7 is a schematic representation of a microelectrode system according to the invention forming an impedance imaging system; and

Figures 8a and 8b illustrate preferred embodiments of microelectrodes of the invention.

Referring to Figure 1a, a microelectrode system 1 comprises alternating layers of conductor 3 and dielectric (or insulator) 4. The laminated structure 2 comprises two conductor layers 3 and two dielectric layers 4 formed on a base 5 of silicon or a polymeric material. The conducting layers 3 form electrodes in the microelectrode system 1. The laminated structure has formed within it an aperture in the form of a well 6 being open at one end 7 and closed at the opposite end 8.

The microelectrode system 10 shown in Figure 1b has formed within the laminated structure 2 a through hole 11 and comprises three dielectric layers 4 and two conducting layers 3.

Figures 2a and 2b illustrate microelectrode systems 20 and 30 respectively which are similar to the microelectrode systems 1, 10 with similar reference numerals retained to avoid confusion. Each of the microelectrode systems 20, 30 comprises three conducting (electrode) layers 3 and three dielectric layers 4. Hole 11 (Figure 2b) or well 7 (Figure 2a) define an internal wall formed from alternating layers of insulating and conducting material. This produces a circular micro-band microelectrode system in the form of a uniform tube. This can be seen more clearly with reference to Figure 3 which is a

three-dimensional representation of the microelectrode system 10 of Figure 1b.

Materials passing into the structure may be pre-treated. A system suitable for pretreatment of material is shown in Figures 4a and 4b (where parts equivalent to those in Figures 1a and 1b have been given equivalent reference numerals). The microelectrode systems 50, 60 contain two electrode layers 3, two dielectric layers 4 and a reagent loaded or functionalised dielectric layer 5. The reagent loaded or functionalised dielectric layer 5 is able to provide additional functionality by providing ions or other materials to ensure the reproducible behaviour of subsequent systems within the structure. Ions could be provided by ion exchange resin materials. Other matrices could be employed to provide co-factors for biosensors, etc. The layer 5 could act as a buffer if, for example, there was some kind of ion exchange taking place where a remote reservoir was replenishing the ions exchanged within the medium in contact with the membrane.

Referring now to Figure 5a and 5b, a microelectrode system according to the invention is designated generally by the reference numeral 70 with parts equivalent to those shown in Figure 1b given equivalent reference numerals. The microelectrode system 70 comprises a specialised layer 13 between two electrode layers 3. The system further comprises means 14 to produce physical or chemical gradients or potentials to the specialised layer 13. The specialised layer 13 may be in the form of an ion exchange resin, gel or solid electrolyte. In such a system 70 mass transport from one lateral region of the structure to another may be effected by, for example, osmosis, electro-osmosis, electrophoresis, electrochromatography, ion migration, etc. Reverse flow and counter current techniques may be employed to effect changes in process flows including *inter alia* deionisation.

In Figure 6, a microelectrode system 80 suitable for use in deionisation of a solution is designated generally by the

reference numeral 80. The microelectrode system 80 comprises a plurality of wells 82. Each of the wells 82 is split into pairs by the presence of a continuous layer 84 which serves as a common well bottom for each pair. The well bottom is formed from an ion exchange material. Electrodes on either side of the well-bottom generate a potential gradient which forces ions to move across the membrane. This system may be used to deionise water.

Figure 7 illustrates a microelectrode system suitable for impedance imaging (*eg* mammography). It comprises alternating conducting 3 and dielectric layers 4 with a gold overplating 71 which is contactable with the skin for example. It is not important in this embodiment for the overplating material to contact in the centre of the hole. The overplating adopts a shape according to local variations in the environment. Provided the plating extends beyond the hole or well to the upper surface thereby allowing electrical contact to be made with an external surface, the shape and size is not critical. The overplating may be applied by standard electroplating methods (electrochemical methods).

Figures 8a and 8b illustrate embodiments of the invention of the hole-type and well-type respectively. Dielectric layers are made from poly(ethylenetetraphthalate) and conducting layers from gold. The detailed construction of each embodiment is given in the following tables (typical ranges are given for illustrative purposes only):

1) Hole Structure (Figure 8a)

Dimensions (in microns):

Description	Letter	Dimension	Typical Range
Aperture	A	5	0.5 - 500

Description	Letter	Dimension	Typical Range
First dielectric layer	B	5	1 - 1000
First conducting layer	C	3	0.5 - 500
Second dielectric layer	D	5	0.5 - 1000
Second conducting layer	E	3	0.5 - 500
Third dielectric layer	F	5	1 - 1000

2) Well structure (Figure 8b)

Dimensions (in microns):

Description	Letter	Dimension	Typical Range
Aperture	A	5	0.5 - 500
First Dielectric layer	B	5	1 - 1000
First conducting layer	C	3	0.5 - 500
Second dielectric layer	D	5	0.5 - 1000
Second conducting layer	E	3	0.5 - 500
Third dielectric layer	F	55	1 - 10000

CLAIMS:

1. A microelectrode system comprising a laminated structure having at least one conducting layer capable of acting as an electrode, at least one dielectric layer, an aperture formed in the laminated structure, and contact means for allowing electrical contact with at least one conducting layer.

2. A microelectrode system as claimed in claim 1 wherein said aperture defines a uniform or non-uniform internal wall in the laminate structure.

3. A microelectrode system as claimed in claim 1 or 2 wherein said aperture defines a substantially tubular internal wall in the laminate structure.

4. A microelectrode system as claimed in any preceding claim comprising a plurality of apertures.

5. A microelectrode system as claimed in any preceding claim wherein said aperture is a through hole which extends through the laminated structure and is open at both ends.

6. A microelectrode system as claimed in any of claims 1 to 4 wherein the aperture is in the form of a well having an open end and an opposite end being closed to form a well bottom.

7. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer is functionalised.

8. A microelectrode system as claimed in any preceding claim wherein at least one dielectric layer is made from a

rubbery material having a solid state matrix capable of swelling in the presence of a liquid or gas.

9. A microelectrode system as claimed in any preceding claim wherein consecutive conducting layers are separated by dielectric layers.

10. A microelectrode system as claimed in any preceding claim wherein the laminate structure is constructed on a base comprising silicon or a polymeric material.

11. A microelectrode system as claimed in any preceding claim comprising at least one pair of substantially collinear wells having a common well bottom.

12. A microelectrode system as claimed in claim 11 comprising a plurality of pairs of substantially collinear wells having a common well bottom.

13. A microelectrode system as claimed in claim 11 or 12 wherein said well bottom is formed from an ion exchange material.

14. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer is metallic and treated with an organic conducting layer.

15. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer is a silver/silver chloride reference electrode.

16. A microelectrode system as claimed in any preceding claim wherein at least one conducting layer consists essentially of gold.

17. A microelectrode system as claimed in claim 16, wherein at least one dielectric layer is polymeric and acts as a support for the gold conducting layer.

18. A microelectrode system as claimed in any preceding claim comprising means for assisting mass transport.

19. A microelectrode system as claimed in claim 18 wherein said means for assisting mass transport is a piezoelectric vibrator or ultrasonic probe.

20. A microelectrode system as claimed in any preceding claim comprising alternating conducting and dielectric layers.

21. A microelectrode system as claimed in any preceding claim wherein at least one dielectric layer comprises a specialised layer in the form of an ion exchange resin, gel or solid electrolyte.

22. A microelectrode system as claimed in claim 21 wherein the specialised layer is provided with means to apply physical or chemical gradients or potentials thereto.

23. A microelectrode system as claimed in any preceding claim wherein at least one dielectric layer comprises a reagent loaded or functionalised layer.

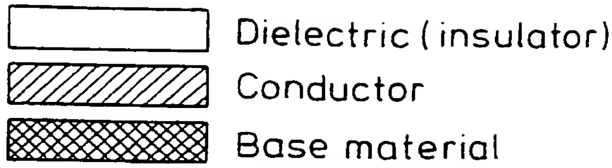
24. Use of a microelectrode system as claimed in any preceding claim for deionisation of a material.

25. Use of a microelectrode system as claimed in any of claims 1 to 23 for use in preparative electrochemistry.

26. Use of a microelectrode system as claimed in any of claims 1 to 23 for use in electroanalysis.

27. Use of a microelectrode system as claimed in any of claims 1 to 23 for use as a sensor.

28. Use of a microelectrode system as claimed in any of claims 1 to 23 for use in chromatography or separation techniques.



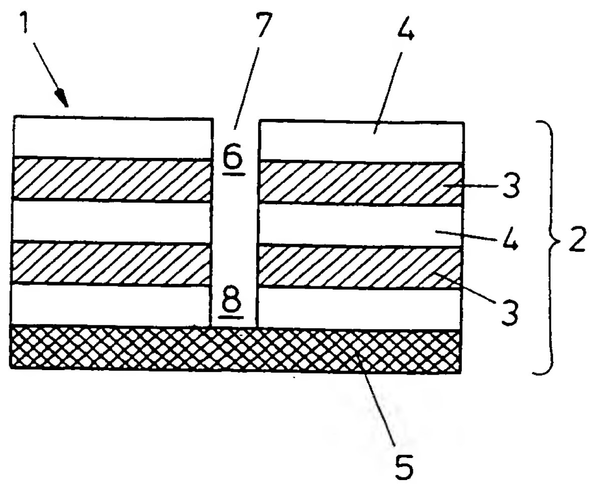


FIG. 1a

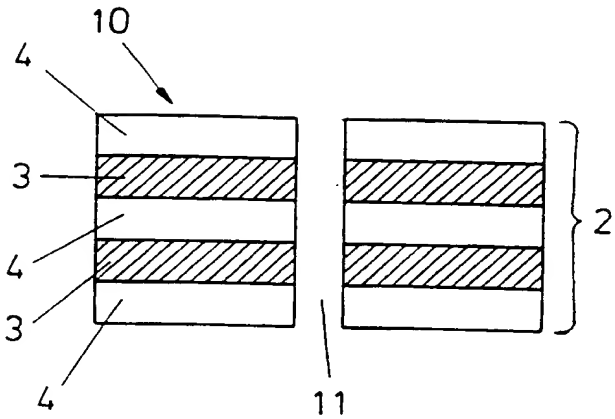
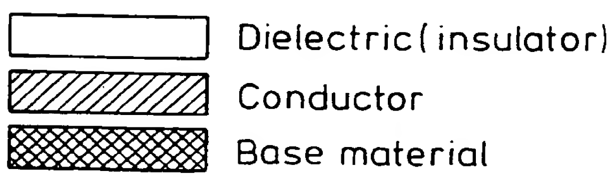


FIG. 1b



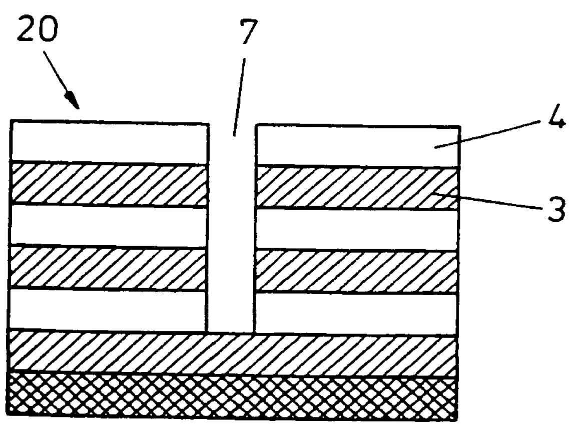


FIG. 2a

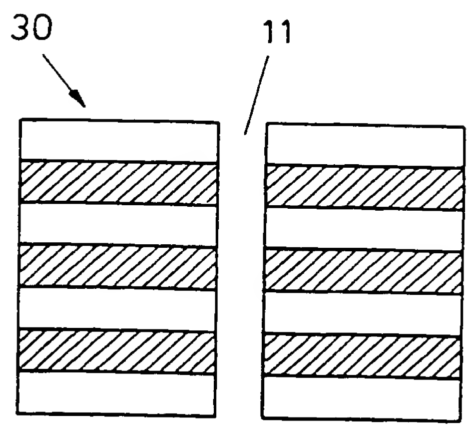


FIG. 2b

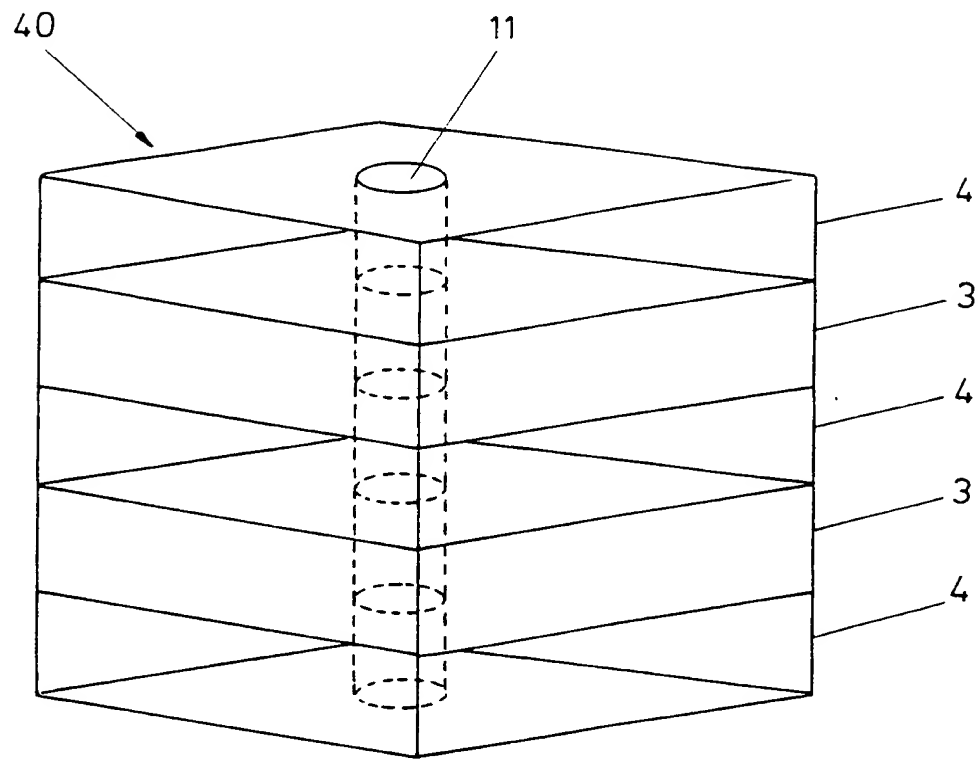
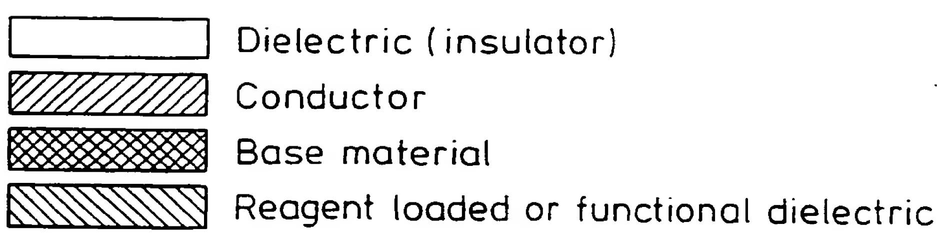


FIG. 3



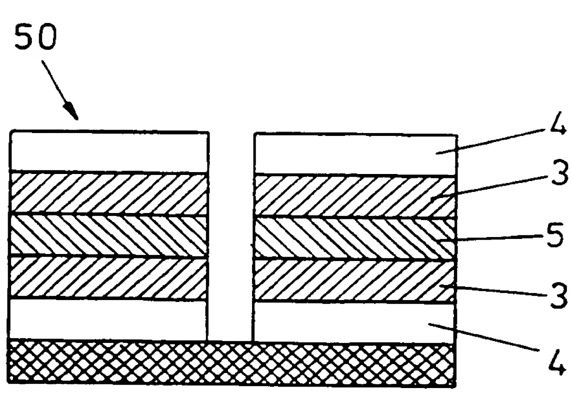


FIG. 4a

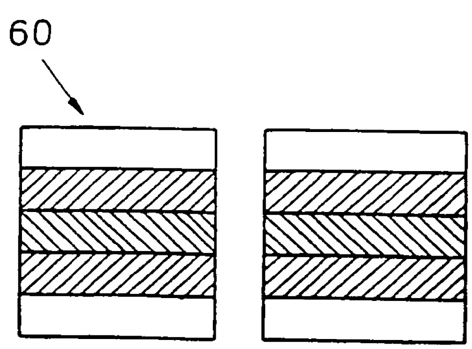


FIG. 4b

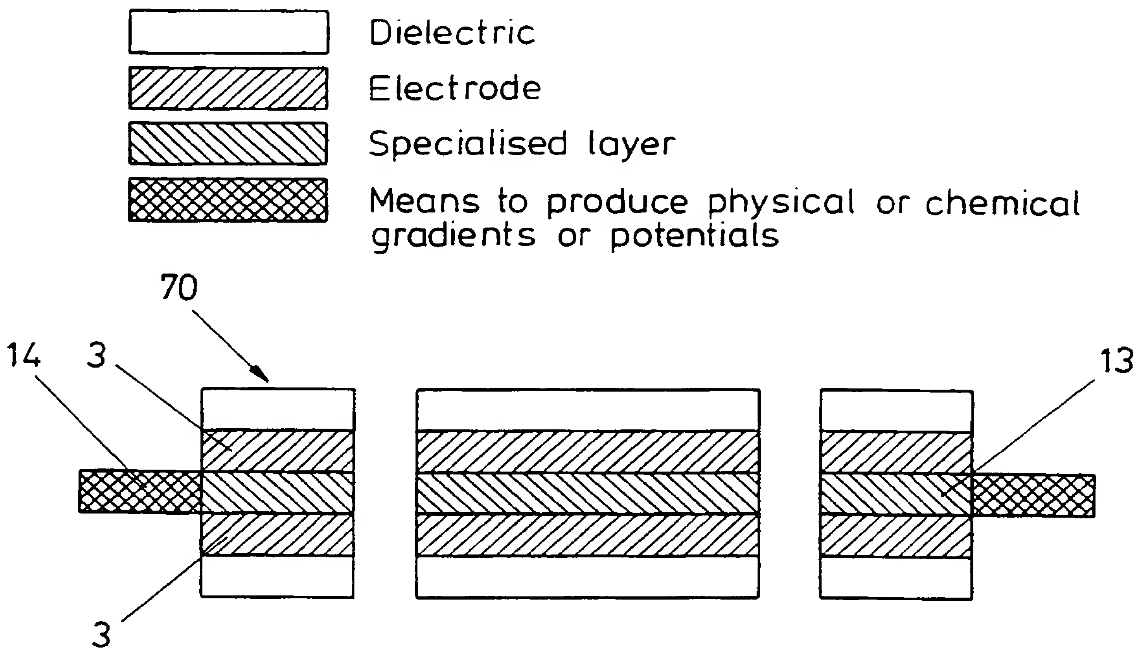

Dielectric
Electrode
Specialised layer
Means to produce physical or chemical gradients or potentials
70
14
3
13
3

FIG. 5a

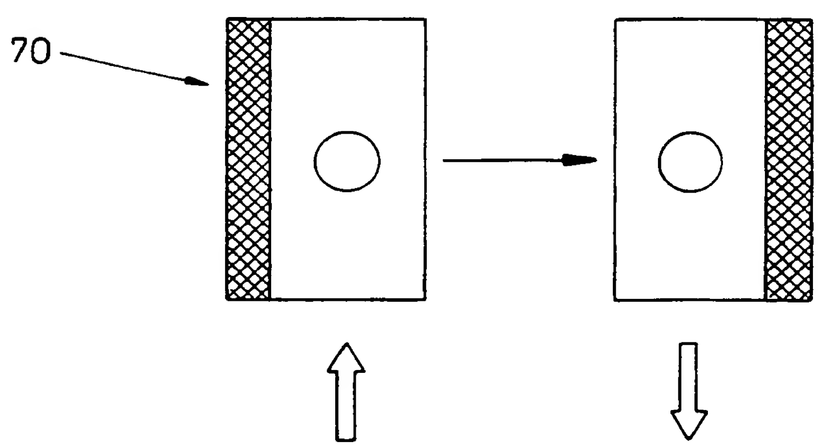

70

FIG. 5b

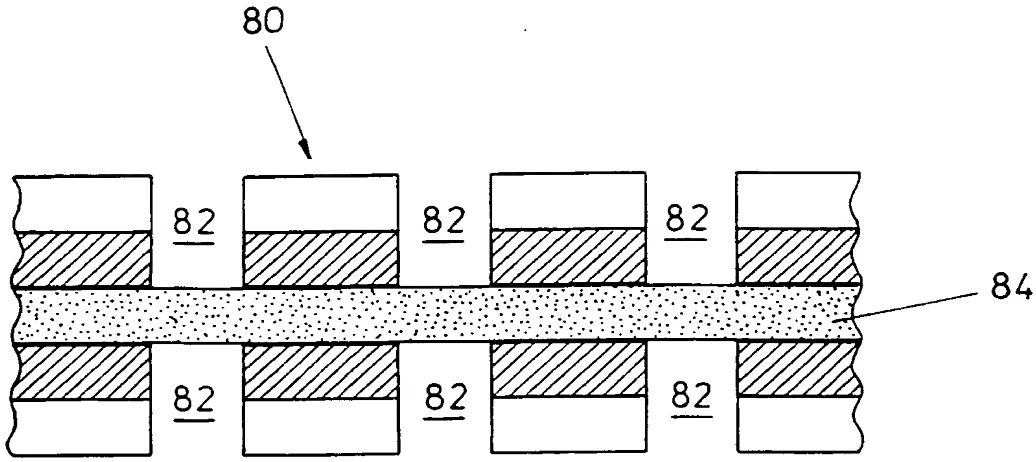


FIG. 6

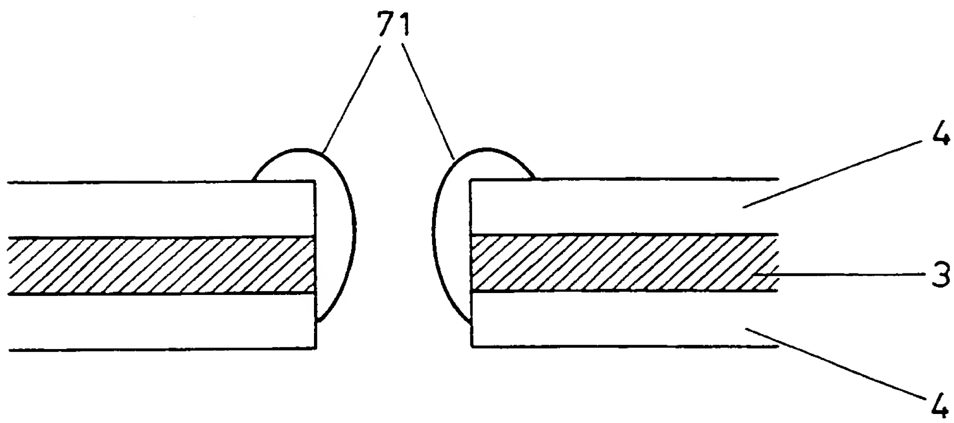


FIG. 7

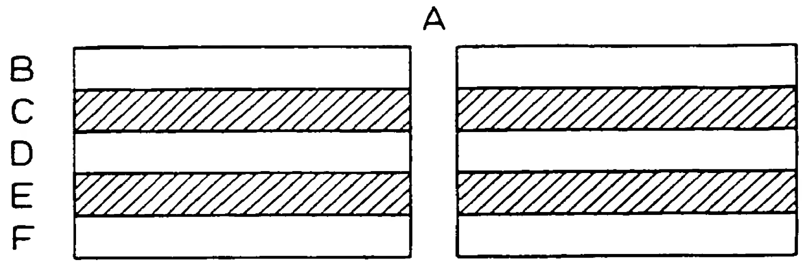


FIG. 8a

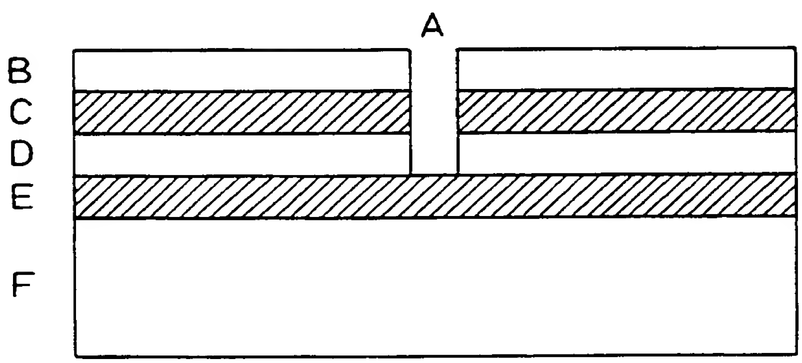


FIG. 8b

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/01379

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N27/403

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 September 1999	15/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Johnson, K

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Form PCT/ISA/210 (second sheet) (July 1992)

International Application No
PCT/GB 99/01379

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	page 399, left-hand column, paragraph 2 - right-hand column, line 4, paragraph 3; figure 1	5,15
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P,X	US 5 824 494 A (FELDBERG S) 20 October 1998 (1998-10-20) column 10, line 33 - line 64; figure 8	1-5,9,26

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 99/01379

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